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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/802,397 | 03/09/2001 | Muriel Moser | DECLE55.1CP2DV | 7548 |

20995 7590 04/25/2005

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| EXAMINER | |
|---|---|
| EWOLDT, GERALD R | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | |

DATE MAILED: 04/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/802,397 | MOSER ET AL. | |
| | Examiner | Art Unit | |
| | G. R. Ewoldt, Ph.D. | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,5,7,9,11,13,15,17,21,23,29,38,51 and 52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,7,9,11,13,15,17,21,23,29,38,51 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

**DETAILED ACTION**

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 2/07/05 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendment, remarks, and second declaration of Inventor Moser, filed 2/07/05, have been entered.

2. Claims 1, 5, 7, 9, 11, 13, 15, 17, 21, 23, 29, 38, and newly added Claims 51 and 52 are pending and are being acted upon.

3. In view of the instant amendments all previous rejection under 35 U.S.C. 103(a) have been withdrawn because there is no teaching in Sornasse et al. of proliferating DCs as the preferred APCs. Additionally, in view of the instant amendments, the previous rejections under the first and second paragraphs of 35 U.S.C. 112 have also been withdrawn.

4. The following are new grounds for rejection.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 5, 7, 9, 11, 13, 15, 17, 21, 23, 29, 38, and newly added Claims 51 and 52, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that a DC hybrid comprising a proliferating DC would be capable of producing an anti-tumor response.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without

an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

Regarding novel methods involving biological processes, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)". The MPEP further states that physiological activity can be considered inherently unpredictable. The state of the immunological arts are such that it is well-documented in the literature that proliferating DCs (and, thus, hybrids comprising proliferating DCs) would not likely be capable of producing an anti-tumor response.

A review of the specification discloses that only hybrid clone 38 of Example 12 was tested for the ability to produce any relevant anti-tumor activity. The clone comprised a fusion employing a DC generated after 10 days in culture with GM-CSF and TNFα. The DCs after culture were MHC Class II+, B7.1+, and B7.2+. There is no disclosure as to whether or not the DCs after 10 days in culture were proliferating or not. Given this combined disclosure, it is more likely than not that the DCs employed in the example were unstable mature DCs, particularly given the expression of costimulatory molecules B7.1 and B7.2 that are more likely to be found on mature, non-proliferating DCs (see, for example, Morelli et al. (2001) which teaches that only mature DCs express B7.2 (CD86), and Shortman et al. (2002) which teaches that mature DCs are non-proliferating). Most

certainly it has not been established that the DCs employed in the experiment were the proliferating DCs of the claims.

As set forth in the second declaration of Inventor Moser, and the remarks of 2/07/05, the proliferating, less differentiated DCs of the claims are immature DCs. There is no evidence of record, however, that an immature DC (and, thus, a DC/tumor hybrid comprising an immature DC) would be capable of producing the required response. The prior art appears to teach the opposite. See, for example, Jonuleit et al. (2000) which teaches that stimulation of naïve T cells with immature DCs results in T cells that are irreversibly proliferation impaired and produce IL-10 (see Results). Dhodapkar et al. extend these findings by showing that immature DCs *in vivo* lead to antigen-specific T cell inhibition (see Results, particularly Figure 2B). Again, the reference teaches that immature DCs would not likely produce an anti-tumor response. Even the Inventors' own work confirms the finding that immature DCs are not inducers of an immune response, see de Heusch et al. 2004 (Figure 3F).

It is the Examiner's position then that the limited disclosure of the instant specification provides insufficient support for the method of the instant claims. Thus, in view of the quantity of experimentation necessary, the lack of any working examples, the unpredictability of physiological activity, and the contrary teachings of the prior art, it would take undue trials and errors to practice the claimed invention.

7. Claims 1, 5, 7, 9, 11, 13, 15, 17, 21, 23, 29, 38, and newly added Claims 51 and 52, are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) A method employing a hybrid... prepared by fusing tumor cells to proliferating dendritic cells... or a method employing "precursors" (Claim 1).

Applicant indicates that support for a proliferating

dendritic cells can be found in paragraph 0184 of the published application.

Applicant's support for the limitation is disclosed only in a specific example in which a particular clone is used in a specific experiment, the results of which are then discussed. Disclosure of a single, specific experiment provides insufficient support for the generic method of the instant claims. Regarding precursors, the specification discloses only dendritic cell precursors.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 23 and 25-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, specifically:

A) "The dendritic cell characteristics" of Claim 5 have no antecedent basis in Claim 1.

B) It is unclear what the additional limitation of Claim 52 is intended to mean, selecting a hybrid to obtain a hybridoma? Accordingly the claim is considered to be vague and indefinite.

10. No claim is allowed.

11. Applicant's amendment or action necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

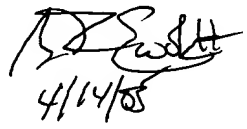
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than

SIX MONTHS from the date of this final action.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

14. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Inquiries of a general nature may also be directed to the Technology Center 1600 Receptionist at (571) 272-1600.

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